TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
NICHI-4		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/001880	09.02.2005	10.02.2004
International Patent Classification (IPC) or national classification and IPC		
C12N15/09, C07K14/47, C12N5/10		
Applicant		
NIHON UNIVERSITY		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:

      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2005/001880

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-13 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 1,10-15,18 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* 2-9,16,17 received by this Authority on 11.08.2006

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets fig. 1 as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-4, 7-18	YES
	Claims	5, 6	NO
Inventive step (IS)	Claims		YES
	Claims	1-18	NO
Industrial applicability (IA)	Claims	1-18	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: J. Exp. Med., 1988, Vol. 167, pages 1975 to 1980

Document 2: Proc. Natl. Acad. Sci. USA., 1988, Vol. 85, pages 208 to 212

Document 3: EP 330191 A2

Document 4: EMBO J., 1988, Vol. 7, No. 3, pages 711 to 717

Document 5: J. Immunol., 1988, Vol. 141, No. 12, pages 4388 to 4394

Document 6: Biochem. Biophys. Res. Commun., 2002, Vol. 291, pages 567 to 573

Document 7: Masami MURAMATSU and Masaharu SAKAI, "Life Science Series Idenshi Kumikae Jitsuyoka Gijutsu," 2nd series, Kabushiki Kaisha Science Forum, 1981, pages 31 to 34

Document 8: WO 97/31012 A1

Document 9: Biochem. Genet., 1996, Vol. 34, No. 7/8, pages 321 to 341

Document 10: WO 01/34194 A1

Claims 1 to 15

Documents 1 to 5 present the nucleic acid sequence and the amino acid sequence for the CD20 protein in

humans and/or mice. Meanwhile, the technique for using the nucleic acid sequence of a gene that is known in a given species in order to design probes and primers for cloning similar genes in other species is well known. Furthermore, in the pertinent technical field it is common practice to use such probes and primers to investigate nucleic acid sequences, and it is also common practice to establish optimal reaction conditions; therefore, it would have been easy for a person skilled in the art to acquire the canine CD20 gene given the disclosures in documents 1 to 5 and the abovementioned well-known technique.

In addition, if it is possible to acquire the gene in question, then a person skilled in the art could prepare a recombinant vector wherein the DNA or RNA of said gene has been linked to the DNA or RNA of a gene that is highly homologous thereto, could prepare a transformant that carries said vector, and could produce both canine CD20 proteins and proteins that are highly homologous thereto by culturing said transformant, as appropriate according to necessity.

With regards to the features in question, in the written response the applicant asserts that "however, it is not necessarily possible to obtain the nucleic acid sequence of the gene in a target species by means of such a method, and thus it cannot be said to be easy to conceive of the inventions set forth in claims 1 to 4. For example, persons skilled in the art would naturally be aware that when attempting to obtain the nucleic acid sequence of a prescribed gene in a target species by means of PCR, there are cases when the target nucleic acid sequence cannot be amplified despite the use of a

primer designed using the nucleic acid sequence of said gene from another highly homologous species and/or the use of reaction conditions that were successful when applied to another highly homologous species." However, although there are cases in which the desired DNA cannot be amplified, as is asserted by the applicant, there are many more cases in which the desired DNA can be amplified in this manner, and thus the abovementioned assertion made by the applicant has no effect upon the abovementioned findings with regards to whether the inventions involve an inventive step.

In the written response, the applicant goes on to assert that the canine CD20 protein is not immunogenic relative to the anti-human CD20 antibody; that canine CD20 protein-specific antibodies are necessary in order to immunize against the canine CD20 protein; and that for these reasons, it cannot be said to be easy for a person skilled in the art to conceive of the effects of the inventions set forth in the present application from the disclosures in documents 1 to 7. In general, however, antigen-antibody reactions are highly specific, and thus a person skilled in the art would expect the canine CD20 protein not to be immunogenic relative to the anti-human CD20 antibody, and would also expect that canine CD20 protein-specific antibodies will be necessary in order to immunize against the canine CD20 protein; therefore, the inventions set forth in the present application cannot be found to exhibit effects that would have been impossible to predict.

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Claims 5 and 6

Documents 1 to 5 present the nucleic acid sequence and the amino acid sequence for the CD20 gene in humans and/or mice, and a comparison of the nucleic acid sequences of the genes in question and the nucleic acid sequence of the canine CD20 gene demonstrated that these nucleic acid sequences have a homology of 80% or higher; therefore, claims 5 and 6 merely set forth the inventions that are disclosed in documents 1 to 5.

Claims 16 to 18

It would have been easy for a person skilled in the art to conceive of designing a primer for amplifying the canine CD20 gene or a fragment thereof from the genes that were acquired based on the disclosures in documents 1 to 7. Furthermore, it is apparent from the disclosures in document 10 that the CD20 protein is an antigen that exhibits elevated expression levels in patients suffering from malignant lymphoma; therefore, it would have been easy for a person skilled in the art to conceive of using the primer for amplifying the canine CD20 gene or a fragment thereof which was acquired based on the disclosures in documents 1 to 7 in a technique for diagnosing malignant lymphoma.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*